# 60°-11-087 CIPI (sheet 1 ) f 52) Figure 1

NTATTGCTGAGCTCAGGGAGTGAGGGCCCCACATTTGAGACAGTGAGCCCCAAGAAGAGG	60
CATCCCTGCTCCAGCAGCTGCAAGGTGCAAGAAGAAGAAGAACATCCCAGGGAAGGAA	120 2
CTGGAGACCCCTGTGCGTTCCTGTGGCTTTGGTCCTATCTGTCTATGTTCAAGCAGT	180 22
CCCTATCCAGAAAGTCCAGGATGACACCCAAAACCCTCATCAAGACCATTGTCACCAGGAT	240 42
CANTGACATTICACACACGCAGTCGGTTATCCGCCAAGCAGAGGGTCACTGGCTTGGACTT	300 62
CATTCCTGGGCTTCACCCATTCTGAGTTTGTCCAAGATGGACCAGACTCTGGCAGTCTA  1 P G L H P I L S L S K M D Q T L A V Y	360 82
TCAACAGGTCCTCACCAGCCTGCCTTCCCAAAATGTGCTGCAGATAGCCAATGACCTGGA	420 102
CAATCTCCGAGACCTCCTCCATCTGCTGGCCTTCTCCAAGAGCTGCTCCCTGCCTCAGAC N L_R_ D L L H L L A F S K S C S L P Q T	480 122
CAGTGGCCTGCAGAGCCCAGAGGGCTGGATGGCGTCCTGGAAGCCTCACTCTACTCCAC S G L Q K P E S L D G V L E A S L Y S T	540 142
AGAGGTGGTGGCTTTGAGCAGGCTGCAGGGCTCTCTGCAGGACATTCTTCAACAGTTGGA B V V A L S R L Q G S L Q D I L Q Q L D	600 162 .
TGTTAGCCCTGAATGCTGAAGTTTCAAAGGCCACCAGGCTCCCAAGAATCATGTAGAGGG	660 167
AAGAAACCTTGGCTTCCAGGGGTCTTCAGGAGAGAGAGAG	720
TCATTTCTCTCCCTCCTGTAGACCACCCATCCAAAGGCATGACTCCACAATGCTTGACTC	780
NAGTTATCCACACAACTTCATGAGCACAAGGAGGGGCCAGCCTGCAGAGGGGACTCTCAC	840
	900
CTAGTTCTTCAGCAAGTAGAGATAAGAGCCATCCCATCC	
GGGTACATGTTCCTCCGTGGGTACACGCTTCGCTGCGGCCCAGGAGAGGGTGAGGTAGGGA	960
TGGGTAGAGCCTTTGGGGTGTCTCAGAGTCTTTGGGAGCACCGTGAAGGCTGCATCCACA	1020
CACAGCTGGAAACTCCCAAGCAGCACACGATGGAAGCACTTATTTAT	1080
TATTTTGGATGGATCTGAAGCAAGGCATCAGCTTTTTCAGGCTTTGGGGGTCAGCCAGGA	1140
TGAGGAAGGCTCCTGGGGTGCTGCTTTCAATCCTATTGATGGGTCTGCCCGAGGCAAACC	1200
TAATTTTTGAGTGACTGGAAGGAAGGTTGGGATCTTCCAAACAAGAGTCTATGCAGGTAG	1260
CGCTCAAGATTGACCTCTGGTGACTGGTTTTGTTTCTATTGTGACTGAC	1320
ACGTTTGCAGCGGCATTGCCGGGAGCATAGGCTAGGGTTATTATCAAAAGCAGATGAATTT	1380
TGTCAAGTGTAATATGTATCTATGTGCACCTGAGGGTAGAGGATGTGTTAGAGGGAGG	1440
_	1500
GAAGGATCCGGAAGTGTTCTCTGAATTACATATGTGTGGTAGGCTTTTCTGAAAGGGTGA	
GGCATTTTCTTACCTCTGTGGCCACATAGTGTGGCTTTGTGAAAAGGACAAAGGAGTTGA	1560
CTCTTTCCGGAACATTTGGAGTGTACCAGGCACCCTTGGAGGGGCTAAAGCTACAGGCCT	1620
TTTGTTGGCATATTGCTGAGCTCAGGGAGTGAGGGCCCCACATTTGAGACAGTGAGCCCC	1680
AAGAAAAGGGTCCCTGGTGTAGATCTCCAAGGTTGTCCAGGGTTGATCTCACAATGCGTT	1740
TCTTAAGCAGGTAGACGTTTGCATGCCAATATGTGGTTCTCATCTGATTGGTTCATCCAA	1800
AGTAGAACCCTGTCTCCCACCCATTCTGTGGGGAGTTTTGTTCCAGTGGGAATGAGAAAT	1860
CACTTAGCAGATGGTCCTGAGCCCTGGGCCAGCACTGCTGAGGAAGTGCCAGGGCCCCAG	1920
GCCAGGCTGCCAGAATTGCCCTTCGGGCTGGAGGATGAACAAAGGGGCTTGGGTTTTTCC	1980
ATCACCCCTGCACCCTATGTCACCATCAAACTGGGGGGCAGATCAGTGAGAGGACACTTG	2040
ATGGAAAGCAATACACTTTAAGACTGAGCACAGTTTCGTGCTCAGCTCTGTCTG	2100
TGAGCTAGAGAAGCTCACCACATACATATAAAAATCAGAGGCTCATGTCCCTGTGGTTAG	2160
•	2220
ACCCTACTCGCGGCGGTGTACTCCACCACAGCAGCAGCACCGCACCGGCAGGAAGTACAGTGCT	
GTCTTCAACAGGTGTGAAAGAACCTGAGCTGAGGGTGACAGTGCCCAGGGGGAACCCTGCT	2280
TGCAGTCTATTGCATTTACATACCGCATTTCAGGGCACATTAGCATCCACTCCTATGGTA	2340
GCACACTGTTGACAATAGGACAAGGGATAGGGGTTGACTATCCCTTATCCAAAATGCTTG	2400
GGACTAGAAGAGTTTTGGATTTTAGAGTCTTTTCAGGCATAGGTATATTTGAGTATATAT	2460
AAAATGAGATATCTTGGGGATGGGGCCCAAGTATAAACATGAAGTTCATTTATATTTCAT	2520
AATACCGTATAGACACTGCTTGAAGTGTAGTTTTATACAGTGTTTTAAATAACGTTGTAT	2580
GCATGAAAGAEGTTTTTACAGCATGAACCTGTCTACTCATGCCAGGACTCAAAAACCTTG	2640
GGGTTTTGGAGCÄGTTTGGATCTTGGGTTTTCTGTTAAGAGATGGTTAGCTTATACCTAA	2700
AACCATAATGGCAAACAGGCTGCAGGACCAGACTGGATCCTCAGCCCTGAAGTGTGCCCT	2760
TCCAGCCAGGTCATACCCTGTGGAGGTGAGCGGGATCAGGTTTTGTGGTGCTAAGAGAGG	2820
AGTTGGAGGTAGATTTTGGAGGATCTGAGGGC	2652

GGTTC	CAAGGCCCAA	GAAGCCCA	-TCCTGGGAA	GGAAAATGCA	. 50
TTGGGGAACC	CTGTG-CGGA	TTCTTGTGGC	TTTGGCCCTA	TCTTTTCTAT	100
GTCCAAGCTG	TGCCCATCCA	AAAAGTCCAA	GATGACACCA	AAACCCTCAT	150
CAAGACAATT	GTCACCAGGA	TCAATGACAT	TTCACACACG	CAGTCAGTCT	200
CCTCCAAACA	GAAAGTCACC	GGTTTGGACT	TCATTCCTGG	GCTCCACCCC	250
ATCCTGACCT	TATCCAAGAT	GGACCAGACA	CTGGCAGTCT	ACCAACAGAT	300
CCTCACCAGT	ATGCCTTCCA	GAAACGTGAT	CCAAATATCC	AACGACCTGG	. 350
AGAACCTCCG	GGATCTTCTT	CACGTGCTGG	CCTTCTCTAA	GAGCTGCCAC	400
TTGCCCTGGG	CCAGTGGCCT	GGAGACCTTG	GACAGCCTGG	GGGGTGTCCT >	450
GGAAGCTTCA	GGCTACTCCA	CAGAGGTGGT	GGCCCTGAGC	AGGCTGCAGG	500
GGTCTCTGCA	GGACATGCTG	TGGCAGCTGG	ACCTCAGCCC	TGGGTGCTGA	550
GGCCTTGAAG	GTCACTCTTC	CTGCAAGGAC	T-ACGTTAAG	GGAAGGAACT	600
CTGGTTTCCA	GGTATCTCCA	GGATTGAAGA	GCATTGCATG	GACACCCCTT	650
ATCCAGGACT	CTGTCAATTT	CCCTGACTCC	TCTAAGCCAC	TCTTCCAAAG	700
G	·				701
	•				•

	•														-	
1	Met	His	Trp	Gly	Thr	Leu	Суз	Gly	Phe	Leu	Trp	Leu	Trp	Pro	Tyr	
16	Leu	Phe	Tyr	Val	Gln	Ala	Val	Pro	Ile	Gln	Lys	Val	Gln	Asp	Asp	ŀ
31	Thr	Lys	Thr	Leu	Ile	Lys	Thr	Ile	Val	Thr	Arg	Ile	Asn	Asp	Íle	
46	·Ser	His	Thr	Gln	Ser	Val	Ser	Ser	Lys	Gln	Lys	Val	Thr	Gly	Leu	
61	Asp	Phe	Ile	Pro	Gly	Leu	His	Pro	Ile	Leu	Thr	Leu	Ser	Lys	Met	
76	Asp	Gln	Thr	Leu	Ala	Val	Tyr	Gln	Gln	Ile	Leu	Thr	Ser	Met	Pro	
91	Ser	Arg	Asn	Val	Ile	Gln	Ile	Ser	Asn	Asp	Leu	Glu	Asn	Leu	Arg	
106	Asp	Leu	Leu	His	<b>Val</b>	Leu	Ala	Phe	Ser	Lys	Ser	Cys	His	Leu	Pro	
121	Trp	Ala	Ser	Gly	Leu	Glu	Thr	Leu	Asp	Ser	Leu.	Gly	Gly	Val	Leu	
136	Glu	Ala	Ser	Gly	Tyr	Ser	Thr	Glu	Val	Va1	Ala	Leu	Ser	Arg	Leu	
151	Gln	Gly	Ser	Leu	Gln	Asp	Met	Leu	Trp	Gln	Leu	Asp	Leu	Ser	Pro	
166	Gly	Суз	End				•									<b>≓</b> .

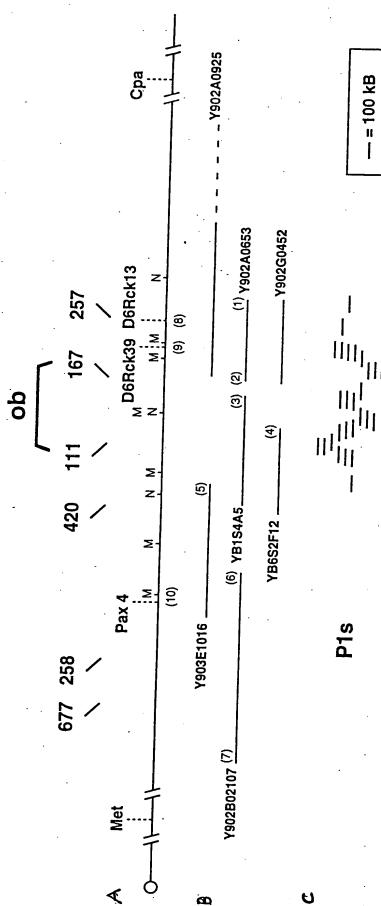
## 201-087 CIPI (she toy of 52)

Mouse	MCWRPLCRFL	MTMZXTZXAO	AVPIQKVQDD	TKTLIKTIVT	KINDISHIDS	30
Human	MHWGTLCGFL	WLWPYLFYVQ	AVPIQKVQDD	TKTLIKTIVT	RINDISHTQS	
Mouse	VSAKQRVTGL	DFIPGLHPIL	SLSKMDQTLA	VYQQVLTSLP	SQNVLQIAND	100
Human	VSSKQKVTGL	DFIPGLHPIL	TLSKMDQTLA	VYQQILTSMP	SRNVIQISND	
Mouse	LENLRDLLHL	LAFSKSCSLP	QTSGLQKPES	LDGVLEASLY	STEVVALSRL	150
Human	LENLRDLLHV	LAFSKSCHLP	WASGLETLDS	LGGVLEASGY	STEVVALSRL	
Mouse	QGSLQDILQQ	LDVSPEC *	•			167
Human	OGSLODMLWQ	LDLSPGC				

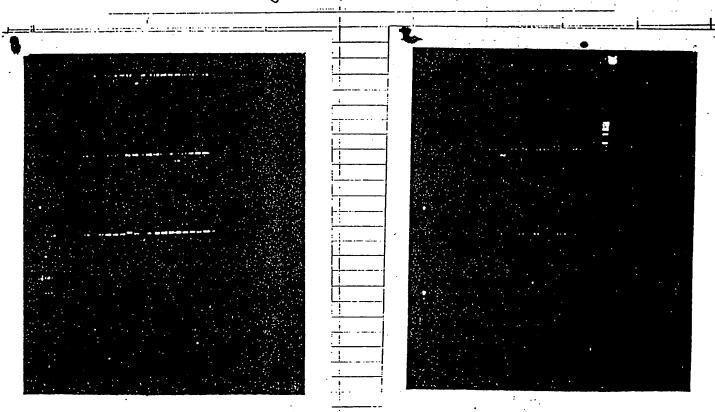
Me	c Cy	Tr	P Arg	7 Pro	Leu	Cys	Arg	r Phe	Leu	Tr	Leu	Trp	Ser	Туг
Let	ı Seı	Tyz	· Val	l Gln	Ala	Val	. Pro	Ile	Gln	Lys	Val	Gln	Asp	Asp
The	Lys	Thr	Leu	ı Ile	Lys	Thr	Ile	Val	Thr	Arg	Ile	Aen	Asp	Ile
Ser	His	Thr	Ser	Val	Ser	Ala	Lys	Gln	Arg	Val	Thr	Gly	Leu	Asp
Phe	Ile	Pro	G1y	Leu	His	Pro	Ile	Leu	Ser	Leu	Ser	Lys	Met	Asn
Gln	Thr	Leu	Ala	Val	Tyr	Gln	Gln	Val	Leu	Thr	Ser	Leu	Pro	Ser
Gln	Asn	Va1	Leu	Gln	Ile	Ala	Asn	Asp	Leu	Glu	Asn	Leu	Ara	: Ban
Leu	Leu	His	Leu	Leu	λla	Phe	Ser	Lys	Ser	Cvs	Ser	Len	Pro	dia
Thr	Ser	Gly	Leu	Gln	Lys	Pro	Glu	Ser	Leu	Aen	Gly	val	T	9111
Ala	Ser	Leu	Tyr	Ser	Thr	Glu	Va l	Val	Ala	T.au	G <sub>2</sub>	AGT	Deu	Gru
G1y	Ser	Leu	Gln	Asp	Ile	Leu	Gla	Gla :			ser	AEG -	ran	din
Cys	End			-			O 1.11	G 144 .	Letu .	web	val	ser	Pro	Ğlu

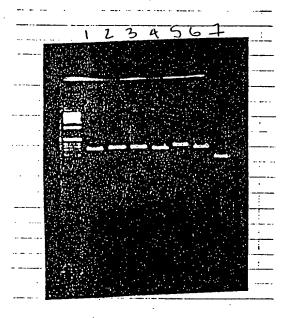
1 Met His Trp Gly Thr Leu Cys Gly Phe Leu Trp Leu Trp Pro Tyr
16 Leu Phe Tyr Val Gln Ala Val Pro Ile Gln Lys Val Gln Asp Asp
31 Thr Lys Thr Leu Ile Lys Thr Ile Val Thr Arg Ile Asn Asp Ile
46 Ser His Thr Ser Val Ser Ser Lys Gln Lys Val Thr Gly Leu Asp
61 Phe Ile Pro Gly Leu His Pro Ile Leu Thr Leu Ser Lys Met Asp
76 Gln Thr Leu Ala Val Tyr Gln Gln Ile Leu Thr Ser Met Pro Ser
91 Arg Asn Val Ile Gln Ile Ser Asn Asp Leu Glu Asn Leu Arg Asp
106 Leu Leu His Val Leu Ala Phe Ser Lys Ser Cys His Leu Pro Trp
121 Ala Ser Gly Leu Glu Thr Leu Asp Ser Leu Gly Cly Val Leu Glu
136 Ala Ser Gly Tyr Ser Thr Glu Val Val Ala Leu Ser Arg Leu Gln
151 Gly Ser Leu Gln Asp Met Leu Trp Gln Leu Asp Leu Ser Pro Gly
166 Cys End





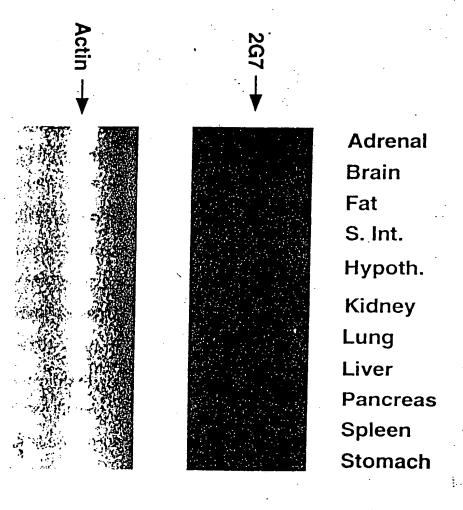
Œ





		+10 AAGAAGATO	+20 CAGGGCÁGG	+30 GA AAATGTGCT	+40 G GAGACCCCTG
1	\$ 44 VIII	+10	+20	+30	C CTCTGGGGAC +40 C AAGCAGTGCC
51	ACAGCCCAGG	?? NCACCNAAAC +10	CAGGATAGA +20 ?	? C AGAATACAN +30	G TTCGTCACGG
101	ATAGGTCTTT	CAGGTCCTAC	TGTGGTTTT		ACCATTGTCA TGGTAACAGT
.151	NCAGGATCAC	TGANATTTCA	+20 CACACG		+40
Indignation (	NGTCCTAGTG	ACTNTAAAGT	GTGTGC		·

Figure 11A



#### Figure 11B

88

white fat

brain

small intestine

stomach

pancreas

lung

testis

heart

spleen

liver

Figure 12A

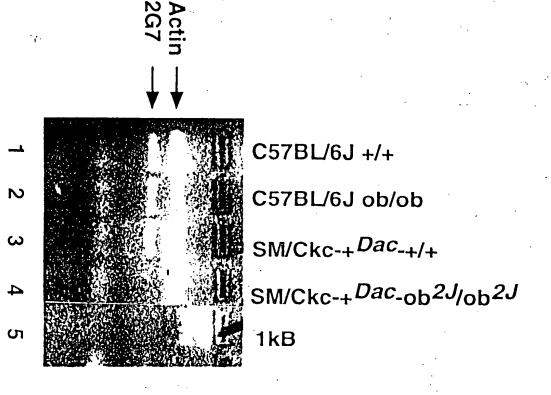


Figure 12 B

SM/Ckc-+*Dac*-+/+ fat SM/Ckc-+*Dac-ob<sup>2J</sup>/ob<sup>2J</sup>* fat C57BL/6J +/+ fat C57BL/6J ob/ob fat

brain

2G7

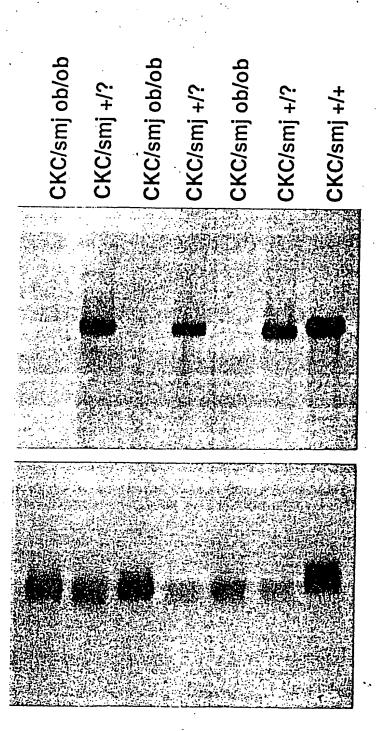
- 28S

**- 18**S

Actin

**- 18**S

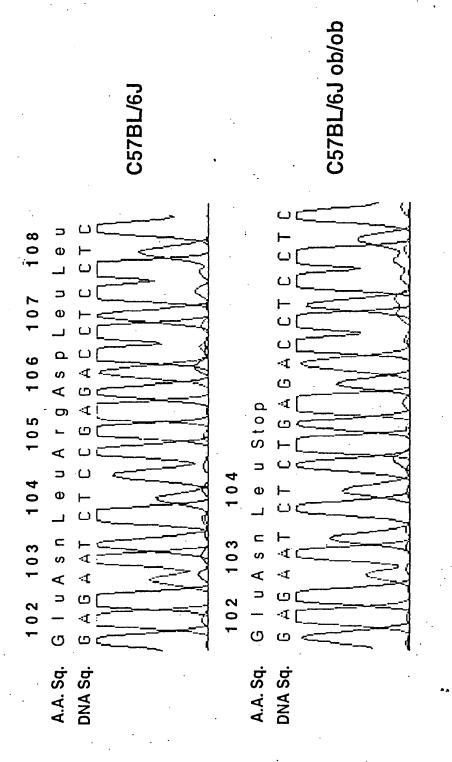
Figure 13



ap2

2G7

Figure 14



#### Figure 15A

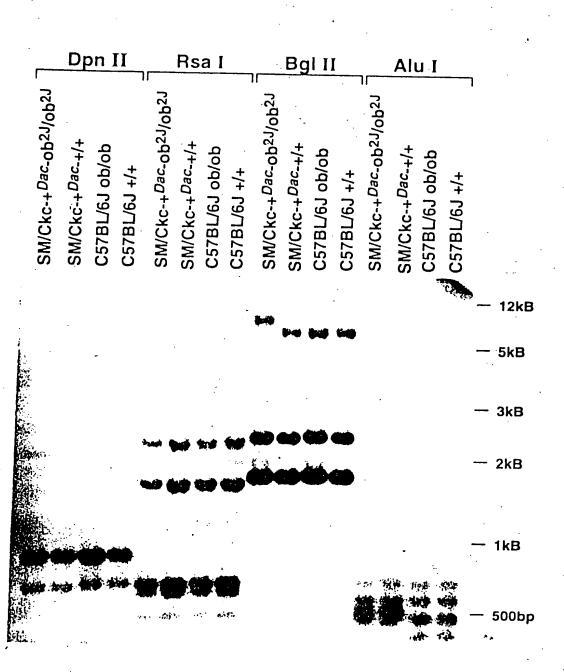
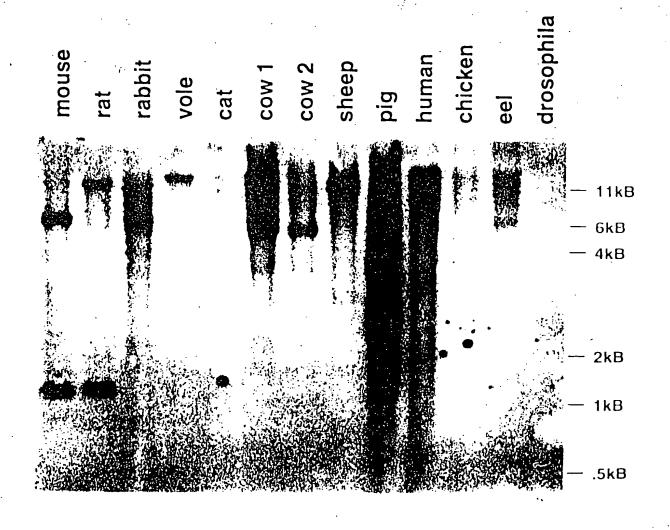


Figure 15B

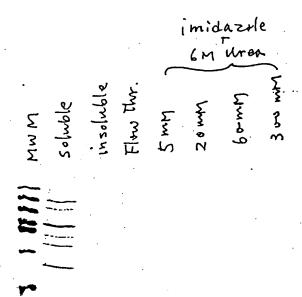
obese special control control



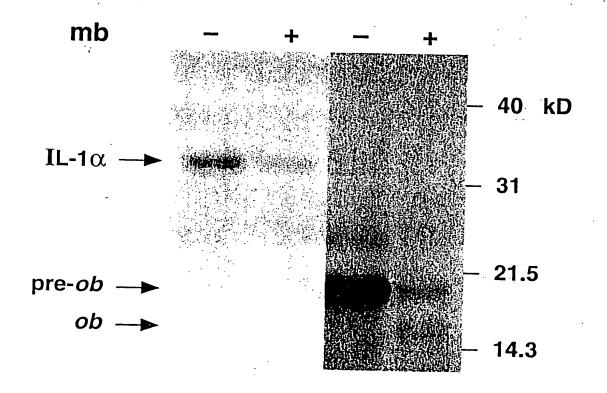
	17 promoter primer #69348-1			
_ <i>Bgl</i> 11	17 promoter	lac operator		
AGATOTOGATOCOGOS	BAAATTAATAEGACTCACTATAGGG		Zba rba TTCCCCCCTAQAAATAATTTTGTTTAACTTTAAGAAGGAG	
	nia*(ag*		Alda i Yha i Comild t	l.
AJDAJDDDTAJJATAT Sregyldfah	AGCCATCATCATCATCACAGCAG Sechighishishishishibili 19ec5e	CCGCCTGGTGCCGCGCGCCA	AGCCATAIGC CGAGGATCCCGCTGCTAACAAAGCCCGA SerhismetleugiuaspproalgalgasnLysAigArg	
	<i>Bpu</i> 11021	thrombin	T7 terminator	
AACCAAGCTGAGTTGG Lysciuaiggiuleua	CTGC GCCACCGCTGAGCAATAACT	AUCATAACCCCTTGGGGCCT	DIIIIIDDDDAATTTTDDDCSAAATTT	
	in neminal or primar in	769337-1	•	

#### Figure 18 A

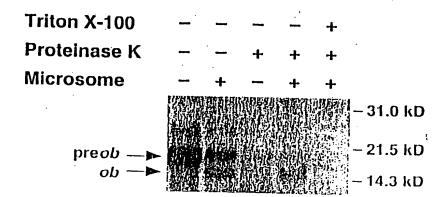
Figure 18B



#### Figure 11A



## Figure 19B ..



	B.A.	we a	M	
10	20	30	4(	50
GGTTGCAAGG	CCCAAGAAGC	CCATCCTGGG		
6,0	HO6 - 9 - 70	8,0	5749 90	5 <sup>T</sup> 190
CCCTGTGCGG	ATTCTTGTGG	CTTTGGCCCT	ATCTTTTCT	TGTCCAAGCT
111	0 120	130	19	0 150
GTGCCCATCC	AAAAAGTCCA	AGATGACACC		TCAAGACAAT
160	170	180	19 5 of 19	est intron
TGTCACCAGG	ATCAATGACA	TTTCACACAC	GTAAGGAGA	GTATGCGGG
2]0	220	230	. 24	0 · 250
ACAAAGTAGA	ACTGCAGCCA	GCCCAGCACT	GGCTCCTAGT	GGCACTGGAC
260	270	280	29	0 HOB19 8300
CCAGATAGTC	CAAGAAACAT	TTATTGAACG	CCTCCTGAAT	GCCAGGCACC
310	320	330	34	0 350
TACTGCAAGC	TGAGAAGGAT	TTTGGATAGC	ACAGGGCTCC	ACTCTTTCTG
360	370	380	39	0 490
GTTGTTTCTT	NTGGCCCCCT	CTGCCTGCTG	AGATNCCAGO	GGTTAGNGGT
410	120	430	44	0 450
TCTTAATTCC	TAAA	AP OF SEQUE	NEW (~ I.	4 Kb) CT
460	470	480	` 49	500
GGTTCTTTCA	GGAAGAGGCC	ATGTAAGAGA	AAGGAATTGA	CCTAGGGAAA
510	T	530	54	
ATTGGCCTGG	GAAGTGGAGG	GAACGGATGG	TGTGGGAAAA	GCAGGAATCT
560	570	580	590	) ရေဝ
CGGAGACCAG	CTTAGAGGCT	TGGCAGTCAC	CTGGGTGCAG	GANACAAGGG
610	620	630	640	650
CCTGAGCCAA	AGTGGTGAGG	GAGGGTGGAA	GGAGACAGCC	CAGAGAATGA
660	670	. 680	690	790
CCCTCCATGC	CCACGGGGAA			ATTCCTCCCA
770	720	3' of 15" 16	TRON	750
	ACTTGTTCTC	CCTCTTCCTC	CTNCATACCA	GTCAGTCTCC
HOB 28 7 760	770	780	790	800
TCCAAACAGA	AAGTCACCGG '	TTTGGACTTC	ATTCCTGGGC	TCCACCCCAT
810	870	830	840	850
CCTGACCTTA	TCCAAGATGG	ACCAGACACT	GGCAGTCTAC	CAACAGATCC
860	870	880	890	
TCACCAGTAT	GCCTTCCAGA Z	AACGTGATCC	AAATATCCAA	CGACCTGGAG

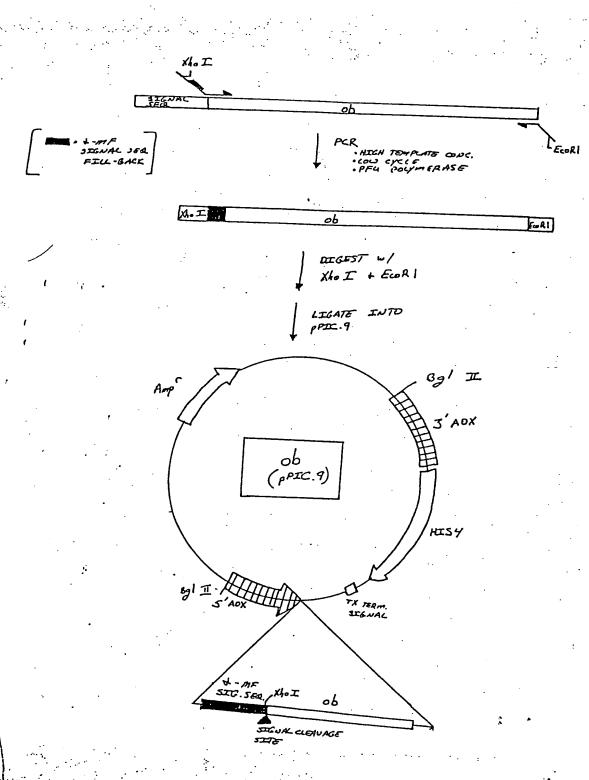
910	920	930	940	950
AACCTCCGGG ATCT	TCTTCA CGT	CTGGCC TTC	CTAAGA GCT	CCACTT
960	970	980	990	1000
GCCCTGGGCC AGTG	GCCTGG AGAC	CTTGGA CAGO	CTGGGG GGTG	TCCTGG
1010	1020	1030	10,40	1050
AAGCTTCAGG CTAC	TCCACA GAGG	TGGTGG CCCT	GAGCAG GCTG	CAGGG
1060	1070	1080	10,90	11,00
TCTCTGCAGG ACAT	GCTGTG GCAG	CTGGAC CTCA	GCCCTG GGTG	CTGAGG
1110	1120	1130	11,40	1150 tupo
CCTTGAAGGT CACT	CTTCCT GCAA	GGACTA CGTT	AAGGGA AGGA	ACTCTG
1160	1170	1180	1190	1200
SCTTCCAGGT ATCT	CAGGA TIGA	AGAGCA TTGC	ATGGAC ACCC	TTATC
1210 H	09291220	. 1230	1240	1250
AGGACTETG TEAAT	TTCCC TGAC	CCTCT AAGC	CACTOT TOCAL	AAGG

## Figure 20B

MOUSE OB STRUCTURE

!st ex	1st intr 2n		2nd intr		
		ATG		************	TGA
	•	start			stop
	•	-	•	<i>:</i>	• • •
,	: ,				-
	, As	/			
			•		
	í	Figure	20c		· · · · · · · · · · · · · · · · · · ·
HUMA	N OB STUC	TURE			
	lst e	xon	1st intr	2nd exon	·
••••••	ATC	}			TGA
•	s	tart			stop

Figure 21A



# Figure 21 B

	XI. I		
<b>///</b>	// LEU-GLU	·LYS · ARG · GLU · ALA · GLU · ALA ·	оЬ
		KEX-2 STE-13 CLEAVAGE CLEAVAGE	
	¥	GLU-ACA-GLU-ACA.	ob
		•	ФÞ

Figure 21 c

- Xh. I.	LYS · ARG ·	
	KEX-2 CLEAVAGE	
· ·	_	

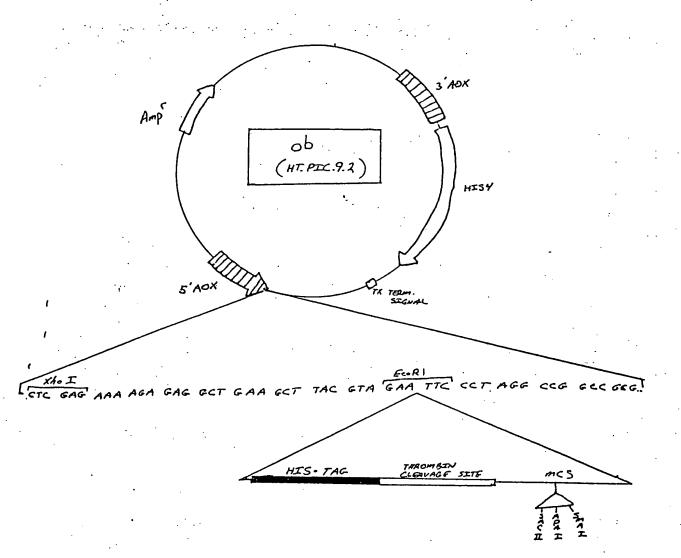


Figure 22B.

W-MF SIG SEC.	, seems	HIS. TAG THROWBIN CLOANACE			<i>o</i> b		
	KET-2 STE-17 KET-2 STE-17 CLENVAGE	y-466		ļ	(FOLIONE THROW BY	THROM BIN CLEANAGE)	
•		·					

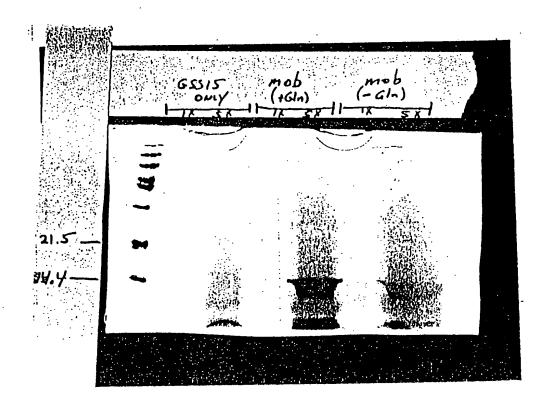


Figure 23B

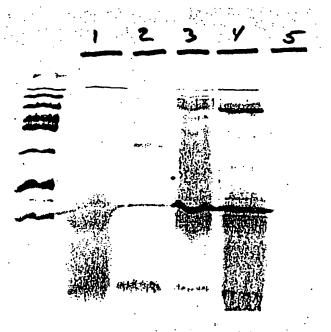


Figure 24 A

Aeast M-ob 121.0 — Veast M-ob 27.8 — Veast M-ob wild type ob/ob 40/db Figure 24B

19.4

Yeast M-ob

Zucker Lean

fa/fa

600-1-087 CIP/ (sheet 34 ot 52)

Figure 24C

recombinant ob (ng)

wt 0.01 0.1 0.5 2.0 15.0

19.4 —

600-1-081 L+11 (sneer 33 0+ 34)

Figure 24 D

9.4

OOSISSSY OSLOCO

Yeast M-ob wild type db/db

## Figure 25A

Yeast H-ob
HP1
HP2
HP3
HP4
HP5
HP6

man 1-001 and 1 (2)

Figure 25 B

## **ELISA STANDARD CURVE**

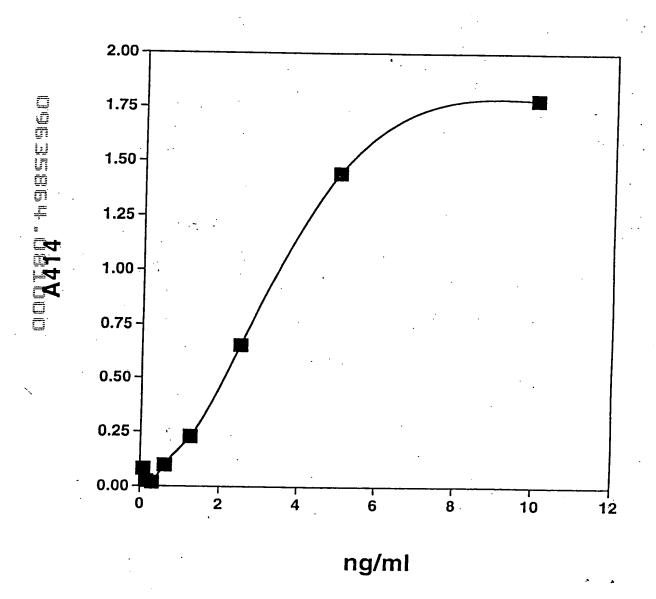
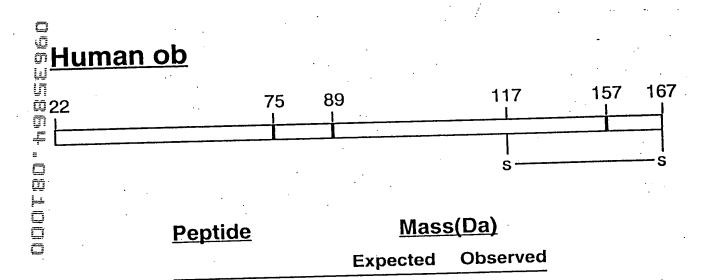
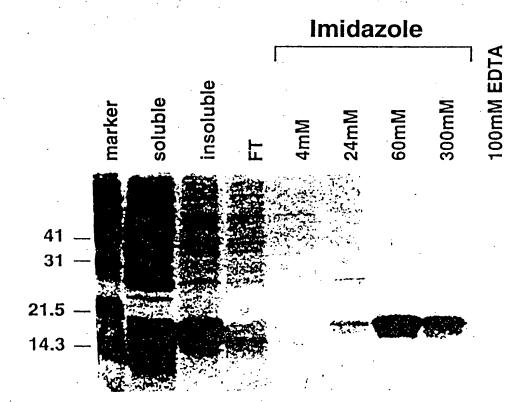


Figure 26 B



<u>Peptide</u>	<u>ivia55(Da)</u>	
·	Expected	Observed
22-167 22-75 76-89 90-167 158-167	16,024 5936.9 1562.7 8434.5 1131.9	16,024 ± 3 5936.6 ± 1 N.D. 8435.6 ± 1 N.D.

## Figure 27



100-1-08, UP1 (Sheet 44 ot 52)

Figure 28 C





600-1-087 CFP1 (sheet 45 of 52)

Figure 28D



osasset .. osloo

Figure 29

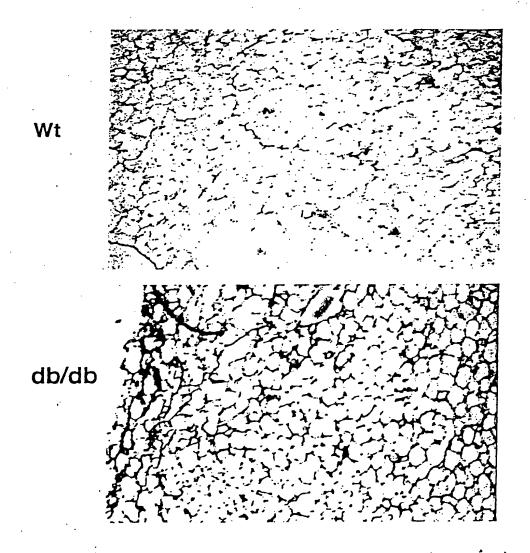
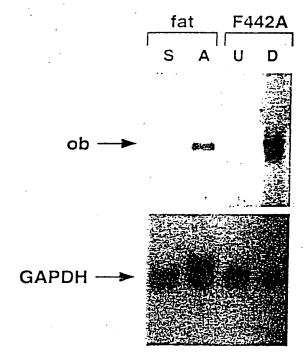


Figure 30



## Figure 31 B

brown fat RNA/RT brown fat RNA @ 4°c

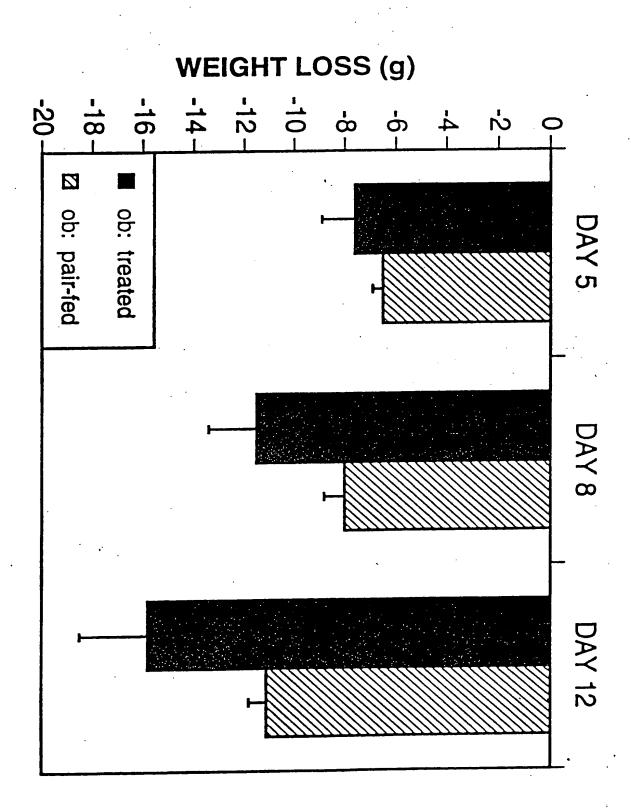


ob



ucp

Figure 28B



## Figure 31 A

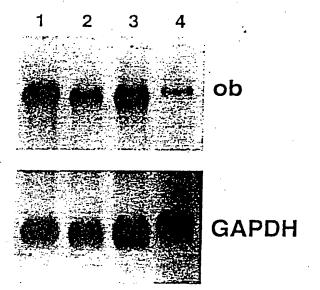


Figure 32

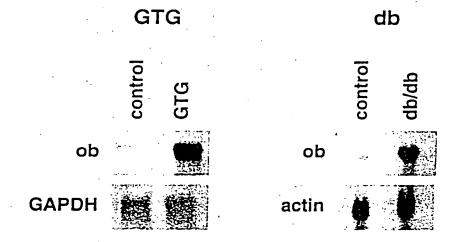
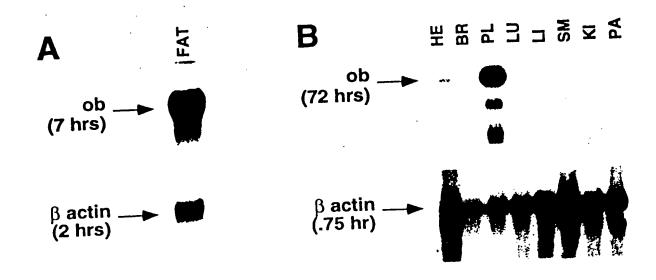


Figure 33



CONTROL HEEREN

Figure 34

